The Journal of Dermatology
Vol. 32: 169–173, 2005

Benzoyl Peroxide, Adapalene, and Their Combination in the Treatment of Acne Vulgaris

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Abstract

Benzoyl peroxide and adapalene are among the most effective topical agents used in the treatment of acne. We planned an open-labeled, prospective study to compare the effects and side effects of these two drugs alone and in combination in the treatment of acne vulgaris. One hundred and five consecutive patients (30 men and 75 women) with acne vulgaris were included in this study. The patients were randomly divided into three groups with 35 patients in each. The groups were randomly assigned to 0.1% adapalene gel, 5% benzoyl peroxide lotion, or combination of 0.1% adapalene gel +5% benzoyl peroxide treatment. Acne lesions were classified as noninflammatory (open and closed comedones) and inflammatory (papule, pustule, nodule, cyst), and the lesions on the face were counted before the therapy, during the control visits, and after the treatment. Erythema, dryness, burning, and other side effects were recorded during the treatment. The mean age of the patients was 18.44 ± 3.75 years. Eight patients were excluded because of noncompliance with the treatment regimen or the follow-up schedule, and four patients were excluded due to allergic contact dermatitis. The study revealed that all three therapy protocols were effective in treating noninflammatory and inflammatory lesions in acne vulgaris ($p<0.05$) and that there was no significant difference between the groups in efficacy or side effects ($p>0.05$). Adapalene and benzoyl peroxide are effective and well tolerated agents for acne vulgaris; combination therapy has no superiority over adapalene or benzoyl peroxide alone.

Key words: acne vulgaris; benzoyl peroxide; adapalene; therapy; side effects

Introduction

Benzoyl peroxide (BP) and adapalene (A) are among the most effective topical agents used in the treatment of acne (1). However, the number of studies that compare the effectiveness of BP and A is small. This study was planned to compare the effects and side effects of these two drugs alone and in combination in the treatment of acne vulgaris and to determine whether or not they have a synergystic effect.

Received July 20, 2004; accepted for publication September 28, 2004.

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Materials and Methods

One hundred and five consecutive patients (30 men and 75 women) seen in outpatient clinics with the diagnosis of acne vulgaris were included in this study.

Patients who had been treated for acne with topical agents, systemic antibiotics, or isotretinoin within the preceding 15 days, one month, or six months, respectively, and those who had severe acne vulgaris according to the acne grading system of the American Academy of Dermatology were excluded (2).

Pregnancy, usage of oral contraceptives or other drugs with possible effects on hormone levels, irregular menstruation, and hirsutismus were other reasons for exclusion from the study. Written consent was taken from all patients participating to the study.

The “lesion counting technique” was used in

Table 1. Mean counts of lesions before and after treatment, reduction ratios of lesions of the treatment groups, and p values

	Noninflammatory lesions				Inflammatory lesions				Total lesions			
	Begin (n±SD)	End (n±SD)	MR (n±SD)	P	Begin (n±SD)	End (n±SD)	MR (n±SD)	P	Begin (n±SD)	End (n±SD)	MR (n±SD)	P
A	93.4±71.9	29.2±23.4	68.8	<0.05	23.9±14.6	10.9±6.0	54.5	<0.05	117.2±78.3	40.1±26.3	65.8	<0.05
BP	90.0±79.3	27.7±22.4	61.0	<0.05	27.7±22.4	7.8±4.7	72.0	<0.05	117.6±89.0	42.8±30.2	63.6	<0.05
ABP	96.8±66.9	25.8±18.7	66.7	<0.05	25.8±18.7	9.1±7.8	64.6	<0.05	122.6±78.3	41.4±28.9	66.2	<0.05

A=0.1% adapalene gel, BP=5% benzoyl peroxide lotion, ABP=0.1% adapalene gel +5% benzoyl peroxide lotion combination, Begin=Mean lesion counts at the beginning of treatment, End=Mean lesion counts at the end of treatment, MR=Mean reduction ratio (%)

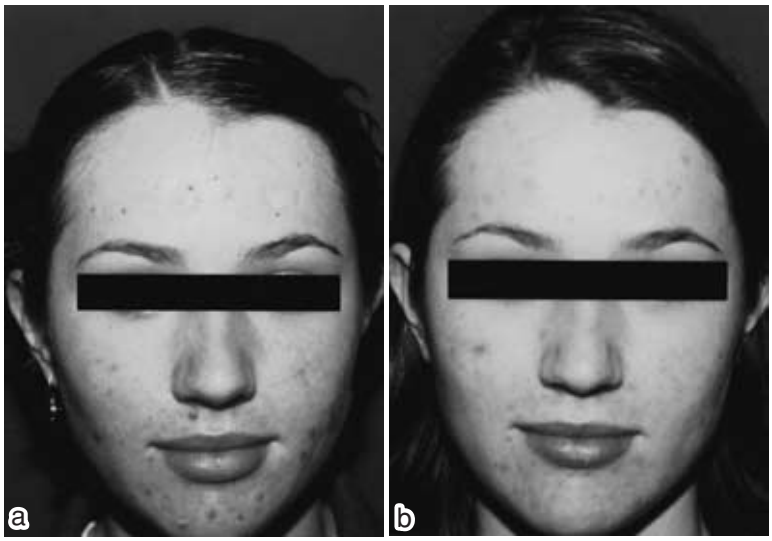

Fig. 1. Pretreatment (a) and post-treatment (b) pictures of a case in group A

order to compare the effectiveness of treatments (3). The lesions were divided into noninflammatory (open and closed comedones) and inflammatory (papule, pustule, nodule, cyst). Lesions on the face were counted; lesions located in other areas were not taken into consideration. The lesions were counted before the therapy, during the control visits, and after the treatment, and pictures were taken from those who gave consent. Erythema, dryness, and burning were evaluated on a four point scale (0=absent, 1=light, 2=moderate, 3=severe). All participants were evaluated for other possible side effects by interviewing and a complete physical examination. Side effects were recorded at each visit.

Patients were randomly divided into three groups with 35 patients in each. 0.1% A gel, 5% BP lotion, or the combination of 0.1% A gel plus 5% BP lotion was given randomly to the groups (group A, group BP, and group ABP, respectively). Treatment duration was planned as six months, and control visits were arranged with one-month intervals. Patients assigned to A or BP alone were instructed to apply the drugs in the evening, whereas patients under combination therapy were instructed to apply A in the evening and BP in the morning. All patients were advised to apply the drugs as a thin layer and to use syndets that have a pH of 5.5 for face cleaning. Patients received no other medication.

The "one way ANOVA test" was used for comparing the efficacy of the treatment protocols. The "paired-samples t-test" was used to evaluate the efficacy of each group; the "Kruskal-Wallis test" was used to compare side effects. $p<0.05$ was accepted as statistically significant.

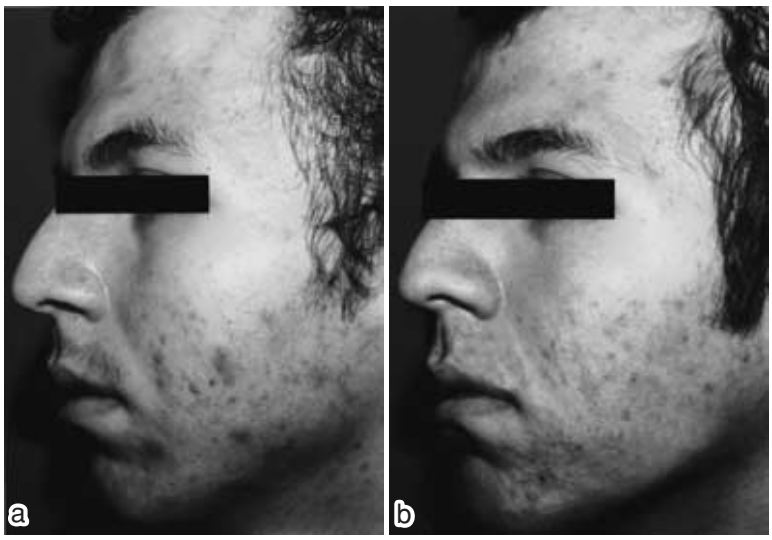

Fig. 2. Pretreatment (a) and post-treatment (b) pictures of a case in group BP

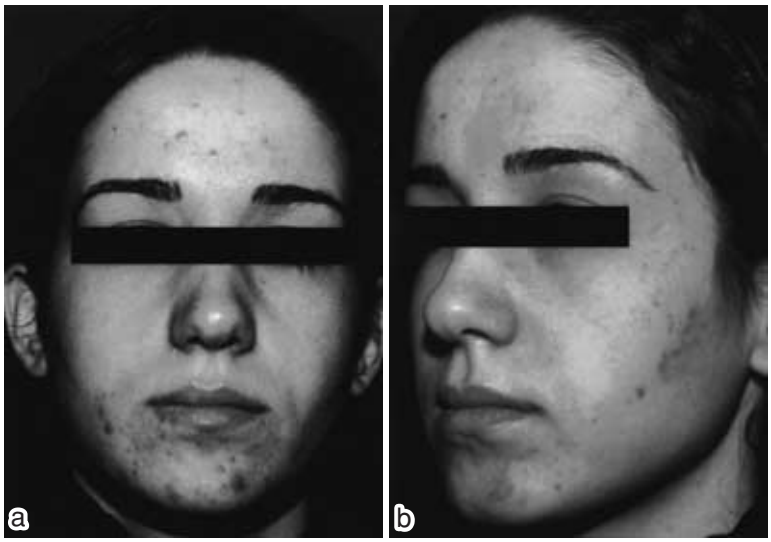

Fig. 3. Pretreatment (a) and post-treatment (b) pictures of a case in group ABP

Results

The mean age of all patients was 18.44 ± 3.75 years (age range 12–32). Eight patients were excluded because of noncompliance with the treatment regimen or the follow-up schedule, and four patients were excluded due to side effects. Ninety-three patients (23 men, 70 women) completed the study.

There were 32 patients (8 men, 24 women) in group A, 29 patients (7 men, 22 women) in group BP, and 32 patients (8 men, 24 women) in group ABP.

There were no significant differences between the groups with regard to the mean values of patient age, disease duration, and initial number of lesions ($p>0.05$).

The results verified that all three therapy protocols were effective in treating noninflammatory and inflammatory lesions in acne vulgaris ($p<0.05$), without any significant differences among the three regimens ($p>0.05$). The mean numbers of lesions before and after treatment, reduction ratios of lesions after treatment, and p values are shown in Table 1. Pre- and post-treatment pictures are presented in Figures 1, 2, and 3.

There were no statistical differences

among the treatment groups with regard to erythema, dryness, and burning ($p>0.05$). These reactions diminished with the continuation of the treatment. Two patients in group BP and two patients in group ABP discontinued the therapy due to acute contact dermatitis.

Discussion

Despite the fact that there are a lot of studies with BP (4, 5) or A (6, 7) alone, there are only a few studies comparing these two drugs. In one of these studies do Nascimento et al. (8) compared the efficacy and safety of 4% BP and 0.1% A on 178 patients after 11 weeks of treatment. They found BP more effective than A on noninflammatory and inflammatory lesions at weeks 2 and 5, and they found both drugs safe.

Ellis et al. (9) researched the efficacy of 0.1% A and 0.025% tretinoin on 297 acne patients. After three months of therapy, they achieved a 57% reduction in noninflammatory lesions, 47% reduction in inflammatory lesions, and 54% reduction in the total lesion counts in the A group.

Cunliffe et al. (10) compared the efficacy of 0.1% A and 0.025% tretinoin on 323 acne patients. They obtained 46% reduction in noniflammatory lesions, 48% reduction in inflammatory lesions, and 49% reduction in total lesion counts in patients treated with A at the end of three months of therapy.

In our study, at the end of the treatment, we found that 0.1% A reduced noninflammatory lesion counts by 68.75%, inflammatory lesion counts by 55.45%, and total lesion counts by 65.48%. According to these results, A was found effective for noninflammatory and inflammatory lesions.

Hughes et al. (11) compared the efficacies of 5% BP, 0.025% isotretinoin, and placebo on 77 patients. After 12 weeks of therapy, 57%, 56%, and 57% reductions in noninflammatory, inflammatory, and total lesion counts, respectively, were observed in patients treated with BP.

Norris et al. (12) examined the efficacies of 5% BP, topical tetracycline and oral oxytetracycline in 69 patients. At the end of three months of therapy, they observed a 58% reduction in noninflammatory lesions, 42% reduction in inflammatory lesions, and 48% reduction in total lesion numbers in patients treated with BP.

In our study, at the end of the therapy, a 61% reduction in noninflammatory lesions, 72% reduction in inflammatory lesions, and 63.6% reduction in total lesion counts was determined. BP was found effective for noniflammatory and inflammatory lesions.

BP is frequently used in combination therapies for acne vulgaris. Especially in combination with topical tetracycline and erythromycin, successful results have been obtained in many studies and furthermore, the reduction of antibiotic resistance was shown with BP combinations (13–17). Handojo (18) used topical 5% BP gel and retinoic acid cream in combination and alone; he reported that the combination therapy was superior.

In our study, at the end of A + BP therapy, a 66.7% reduction in noninflammatory lesions, 64.6% reduction in inflammatory lesions, and 66.2% reduction in total lesion counts were achieved. The combination therapy was found effective for noninflammatory and inflammatory lesions, but there was no statistical difference between the combination therapy and single drug usage.

The majority of patients using BP experience erythema and peeling within the first few days of therapy, but these symptoms resolve in 2–3 weeks. In 2% of patients, allergic contact dermatitis develops due to BP (19).

There are a few studies that compare the side effects of BP and A. Brand et al. (20) found 0.1% A +5% BP combination safe and well tolerated.

In our study, there were no significant differences between the treatment groups in regard to erythema, dryness or burning. The frequency and severity of these side effects decreased during the course of the treatment. Allergic contact dermatitis was

seen in two patients from both the BP and ABP groups, and the therapy was discontinued in these patients. None of the patients discontinued therapy due to adverse effects in group A.

At the end of six months of therapy, all three treatment protocols were found effective on both noninflammatory and inflammatory lesions in acne vulgaris and all three treatment protocols were evaluated as safe and well tolerated. There were no significant difference between treatment groups with regard to efficacy or adverse effects.

We conclude that adapalene gel and benzoyl peroxide lotion are effective and safe in the treatment of acne vulgaris and that the combination of these two remedies has no superiority over single drug therapy with either adapalene or benzoyl peroxide.

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